Quality Control and Good Manufacturing Practices

Good Laboratory Practice (GLP) and Good Manufacturing Practice (GMP)

Scientific codes of practices

A pharmaceutical company's laboratories

A pharmaceutical production plants (factories)

They detail the scientific standards that are necessary and the company must prove to regulatory bodies that it is adhering to these standards.

Good Laboratory Practice (GLP)

It is applied to various research laboratories.

Various laboratories are involved in pharmacology, drug metabolism, and toxicology studies.

Good Manufacturing Practice (GMP)

It is applied to production plants (factories) and chemical development laboratories.

Various laboratories are involved in various manufacturing procedures used in the production of drugs.

It is used to ensure the product is of a high consistent quality.

Good Manufacturing Practice (GMP)

The pharmaceutical company is required to set up an independent quality control unit to monitor a wide range of factors including …

- Employee training
- Working environment
- Operational procedures
- Instrument calibration
- Batch storage
- Labelling
- All solvents intermediates and reagents used In the process

Good Manufacturing Practice (GMP)

Must be detailed and accurate recorded …

- Calibration and maintenance records
- Production reviews
- Batch records and recalls
- Master production records
- Inventories
- Analytical reports
- Equipment cleaning logs
- Customer complaints

Good Clinical Practice (GCP)

Involving clinical research, must demonstrate that all works can be carried out according to GCP.

- Proper staffing

- Facilities

- Equipment for the required work

- Each test site involved

Also demonstrating that the patient's rights and well-being are properly protected.

Effective Cleaning and Maintenance

To avoid cross-contamination

To avoid build-up of dust or dirt

To avoid any adverse (bad) effect on the quality of products

Equipment should be installed to minimize any risk of error or contamination.

Equipment

Must be clearly located; designed; constructed; adapted; and operated.

Fixed pipework should be clearly labelled to indicate the contents and the direction of flow.

Measuring equipment (e.g. balances) should be of an appropriate range and precision, for production and control operations, and calibrated with a properly fixed schedule.

Production equipment should be thoroughly cleaned under properly fixed schedule and procedures.

Washing, cleaning and drying equipment should not be a source of contamination.

Equipment

Avoid any parts being

1. Reactive

2. Additive

3. Absorptive

Equipment

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Chemical and physical properties of the degradation products, if available.

The mechanism and kinetics of degradation products formed, if available.

Equipment

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Sanitation and Hygiene

The scope of sanitation and hygiene covers

Personnel,

Premises,

Equipment and apparatus,

Production materials and containers,

Products for cleaning and disinfection,

Anything that could become a source of contamination to the product.

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Production Areas

To minimize the risk of a serious medical hazard due to contamination …

dedicated and self-contained facilities must be available for the production of particular pharmaceutical products

- Highly sensitizing materials (e.g. penicillins)

- Biological preparations (e.g. living microorganisms)

the production of certain other highly active products should not be conducted in the same facilities

- Antibiotics
- Hormones
- Cytotoxic substances
- certain non-pharmaceutical products

Production Areas

Technical poisons in manufacturing

1. pesticides
2. herbicides
3. not allowed in premise used for pharmaceutical products manufacturing

Think about a logical order corresponding to the sequence of the operations!!!

Quality Control Areas

Areas where biological, microbiological or radioisotope test methods are employed should be separated from each other.

Sufficient space and adequate suitable storage space for

1. samples
2. reference standards
3. solvents
4. reagents
5. records

Quality Assurance and Quality Control

To detect any shortcomings in the implementation of GMP

To recommend necessary actions, involving corrective actions

1. routine

2. on special occasions

Quality Assurance and Quality Control

1. Personnel
2. Premises
3. Maintenance (buildings, equipment, …)
4. Storage
5. Equipment
6. Production and in-process controls
7. Quality control
8. Documentation
9. Sanitation and hygiene

Quality Assurance and Quality Control

10. Validation and revalidation programmes

11. Recall procedures

12. Complaints management

13. Labels control

14. Results of previous self-inspections and any corrective actions taken

Self-inspection report:

1. Inspection result

2. Evaluation and conclusions

3. Recommended corrective actions

Quality Assurance and Quality Control

Concern:

1. Sampling
2. Specifications and testing
3. Organization and documentation
4. Necessary and relevant tests are actually carried out
5. Materials are not released for use
6. Materials (including products) are not released for sale or supply
7. Quality must be judged to be compliant (follow and meet) with the requirement

Quality Assurance and Quality Control

Adequate facilities, trained personnel and approved procedures must be available for

1. sampling, inspecting, and testing starting materials

2. packaging materials

3. intermediate, bulk and finished products

The finished products must contain ingredients complying with the qualitative and quantitative composition of the product described in the marketing authorization.

Quality Assurance and Quality Control

Pay attention:

1. Control of starting materials and intermediate, bulk, and finished products
2. Test requirements
3. Batch record review
4. Stability studies

Labelling

1. Name of the sampled materials
2. Batch or lot number
3. Number of the container(s) from which sample has been taken
4. Number of the sample
5. Signature of the person who has taken the sample
6. Date of sampling

Test requirements

1. Starting and packaging materials
2. In-process control
3. Finished products

Identity test should be conducted on a sample from each container or starting material.

A certificate of analysis has to be accepted from the supplier(s).

- on-site audits of supplier’s capabilities

Test requirements

Certificates must contain:

1. Identification of the issuing supplier (name and address)
2. Signature of the competent official, statement of his/her qualifications
3. Name of the material tested
4. Batch number of the material used
5. Specifications and method(s) used
6. Test results obtained
7. Date of testing

Test requirements

Batch record review:

1. QC records should be reviewed as part of the approval process of batch release before transfer to the authorized person.

2. Any divergence or failure of a batch to meet its specifications should be thoroughly investigated.

3. The investigation should, if necessary extend to other batches of the same product and other products that may have been associated with the specific failure or discrepancy.

4. A written record of the investigation should be made and should include the conclusion and the follow-up action.

Test requirements

Batch record review:

4. Retention samples from each batch of finished product should be kept for at least one year after the expiry date.

5. Finished products should be kept in the final packaging and stored under the recommended conditions.

6. The sample of active starting materials should be retained for at least one year beyond the expiry date of the corresponding finished product.

7. Other starting materials should be retained for a minimum of two years if their stability allows.

8. Retention samples of materials and products should be of a size sufficient to permit at least two full re-examinations.

Stability Studies

Pharmaceutical products

Starting materials

Intermediate products

Stability Studies

A complete description of the medicine involved in the study

The complete set of testing parameters and methods

Provision for the inclusion of a sufficient number of batches

The testing schedule for each medicine

Provision for special storage conditions

Provision for adequate sample retention

A summary of all the data generated, including the evaluation and the conclusions of the study

Stability Studies

To study the stability of the pharmaceutical formulation during its entire shelf-life in its final packaging.

To explain the safety and efficacy of the product during its entire shelf-life.

To study force degradation under stress conditions or accelerated conditions.

Check any changes in – physical, chemical, microbiological, therapeutic properties, any components of the drug which is active or excipients become unstable.

Maintain not less than 90% of its therapeutic activity;

At least 90% of its stated concentration;

An effective concentration of added preservatives;

No observable change, discoloration, precipitation, off odors.

No toxicity and irritancy

Stability Studies

United Stated Pharmacopeia (USP)

Stability is given as the ability of a product to retain its characteristics that is possessed during its manufacturing including physical, chemical, microbiological, therapeutic properties, within specified limits throughout its period of storage and use.

Factors affecting Stabilities Studies

Moisture – water dissolves in contact

Excipients – chemical interaction between the excipients and the drug

Temperature – increase in hydrolysis rate of the drug

pH – rate of decomposition of drugs that are hydrolysed in solution

Oxygen – oxidation

Light – photosensitive, rate of decomposition

Force degradation studies

It is defined as the studies in which stress conditions or accelerated conditions are provided to the drug in bulk or product for two reasons.

1. Developing stability indicating methods specially when there is little information is available for degradation products.

2. Collecting information of the degradation pathways and degradation products which would happen during storage conditions.

Force degradation studies

It facilitates

Pharmaceutical development

Manufacturing and production

Packaging

Chemical behavior can be applied to improve the drug products

Force degradation studies

Stressing the drug substance in solution or suspension at alkaline and acidic pH and under oxidation conditions.

Stressing the solid bulk drug substances at temperature and temperature with humidity conditions in excess of accelerated conditions.

Stressing the drug substance photolytically in the solid state or in solution excess.

Demonstration of the specificity of stability indicating methods with forced degraded samples.

Full characterization of the degraded products by means of NMR, mass spectrometry, and UV analysis.

Chemical and physical properties of the degradation products.

The mechanism and kinetics of degradation products formed.